

1
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NOV 27 2000

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<110> Galdes, Alphonse
Mahanthappa, Nagesh

<120> METHODS AND COMPOSITIONS FOR TREATING DISORDERS INVOLVING
EXCITOTOXICITY

<130> BIV-069.02

<140> 09/325,602

<141> 1999-06-03

<150> 09/238,243

<151> 1999-01-27

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<170> PatentIn Ver. 2.1

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Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg	
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Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
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gcc cac cgc gcc ttc gcc cct ttg cgg ctg ctg cac gcg ctc ggg gct 1104
Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
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Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
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acg ggt gcc gac cgc ctc atg acc cag gcg tgc aag gac cgt ctg aac 336
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Pro	Ala	His	Leu	Leu	Phe	Ile	Ala	Asp	Asn	His	Thr	Glu	Pro	Ala	Ala	
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 Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu Gly Val His Ser Tyr
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 Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr
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 Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn
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 Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp
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aat ccc gac att atc ttt aag gat gag gag aac acg gga gcg gac agg	288
Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg	
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ctc atg aca cag aga tgc aaa gac aag ctg aac tcg ctg gcc atc tct	336
Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser	
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Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp	
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Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg	
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Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu	
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Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu	
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Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp	
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Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val	
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Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu	
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Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr	
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Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys	
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Pro	Asn	Val	Ala	Glu	Lys	Thr	Leu	Gly	Ala	Ser	Gly	Arg	Tyr	Glu	Gly	
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Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg	
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Ser Gly Ser Gly Pro Pro Ser Gly Gly Ala Leu Gly Pro Arg Ala Leu	
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Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu	
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Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr	
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Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu	
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His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp	
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Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser	
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Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu Leu Leu
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Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala Tyr Lys
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tat gaa ggc aag atc gct cgc agc tcc gag cgc ttc aag gag ctc acc      296
Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu Leu Thr
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ccc aat tac aat cca gac atc atc ttc aag gac gag gag aac aca ggc      344
Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly
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gcc gac cgc ctc atg acc cag cgc tgc aag gac cgc ctg aac tcg ctg      392
Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu
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Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr
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Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys
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tat gga ctg ctg gcg cgc ttg gca gtg gag gcc ggc ttt gac tgg gtg      584
Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
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Val	Leu	Ile	Phe	Leu	Asp	Arg	Glu	Pro	His	Arg	Leu	Arg	Ala	Phe	Gln	
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Val	Ile	Glu	Thr	Gln	Asp	Pro	Pro	Arg	Arg	Leu	Ala	Leu	Thr	Pro	Ala	
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cac	ctg	ctc	ttt	acg	gct	gac	aat	cac	acg	gag	ccg	gca	gcc	cgc	ttc	920
His	Leu	Leu	Phe	Thr	Ala	Asp	Asn	His	Thr	Glu	Pro	Ala	Ala	Arg	Phe	
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Arg	Ala	Thr	Phe	Ala	Ser	His	Val	Gln	Pro	Gly	Gln	Tyr	Val	Leu	Val	
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16

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 Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
 1 5 10 15

agc ttg ctt ctg acg cct tgt gga tta gcc tgt ggt cct ggt aga ggt 96
 Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
 20 25 30

tat gga aaa cga aga cac cca aag aaa tta acc ccg ttg gct tac aag 144
 Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
 35 40 45

caa ttc atc ccc aac gtt gct gag aaa acg ctt gga gcc agc ggc aaa 192
 Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
 50 55 60

tac gaa ggc aaa atc aca agg aat tca gag aga ttt aaa gag ctg att 240
 Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
 65 70 75 80

ccg aat tat aat ccc gat atc atc ttt aag gac gag gaa aac aca aac 288
 Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
 85 90 95

gct gac agg ctg atg acc aag cgc tgt aag gac aag tta aat tcg ttg 336
 Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
 100 105 110

gcc ata tcc gtc atg aac cac tgg ccc ggc gtg aaa ctg cgc gtc act 384
 Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
 115 120 125

gaa ggc tgg gat gag gat ggt cac cat tta gaa gaa tct ttg cac tat 432
 Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
 130 135 140

gag gga cgg gca gtg gac atc act acc tca gac agg gat aaa agc aag	480
Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys	
145 150 155 160	
tat ggg atg cta tcc agg ctt gca gtg gag gca gga ttc gac tgg gtc	528
Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val	
165 170 175	
tat tat gaa tct aaa gcc cac ata cac tgc tct gtc aaa gca gaa aat	576
Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn	
180 185 190	
tca gtg gct gct aaa tca gga gga tgt ttt cct ggg tct ggg acg gtg	624
Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val	
195 200 205	
aca ctt ggt gat ggg acg agg aaa ccc atc aaa gat ctt aaa gtg ggc	672
Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly	
210 215 220	
gac cgg gtt ttg gct gca gac gag aag gga aat gtc tta ata agc gac	720
Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp	
225 230 235 240	
ttt att atg ttt ata gac cac gat ccg aca acg aga agg caa ttc atc	768
Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile	
245 250 255	
gtc atc gag acg tca gaa cct ttc acc aag ctc acc ctc act gcc gcg	816
Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala	
260 265 270	
cac cta gtt ttc gtt gga aac tct tca gca gct tcg ggt ata aca gca	864
His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala	
275 280 285	
aca ttt gcc agc aac gtg aag cct gga gat aca gtt tta gtg tgg gaa	912
Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu	
290 295 300	
gac aca tgc gag agc ctc aag agc gtt aca gtg aaa agg att tac act	960
Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr	
305 310 315 320	
gag gag cac gag ggc tct ttt gcg cca gtc acc gcg cac gga acc ata	1008
Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile	
325 330 335	
ata gtg gat cag gtg ttg gca tcg tgc tac gcg gtc att gag aac cac	1056
Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His	
340 345 350	
aaa tgg gca cat tgg gct ttt gcg ccg gtc agg ttg tgt cac aag ctg	1104
Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu	
355 360 365	

atg acg tgg ctt ttt ccg gct cgt gaa tca aac gtc aat ttt cag gag 1152
 Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu
 370 375 380

gat ggt atc cac tgg tac tca aat atg ctg ttt cac atc ggc tct tgg 1200
 Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
 385 390 395 400

ctg ctg gac aga gac tct ttc cat cca ctc ggg att tta cac tta agt 1248
 Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser
 405 410 415

tga 1251

<210> 10
 <211> 425
 <212> PRT
 <213> Gallus sp.

<400> 10
 Met Val Glu Met Leu Leu Leu Thr Arg Ile Leu Leu Val Gly Phe Ile
 1 5 10 15

Cys Ala Leu Leu Val Ser Ser Gly Leu Thr Cys Gly Pro Gly Arg Gly
 20 25 30

Ile Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
 35 40 45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg
 50 55 60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr
 65 70 75 80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly
 85 90 95

Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu
 100 105 110

Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr
 115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr
 130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys
 145 150 155 160

Tyr Gly Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
 165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
 180 185 190

Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val
 195 200 205

His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly
 210 215 220
 Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp
 225 230 235 240
 Phe Leu Thr Phe Leu Asp Arg Met Asp Ser Ser Arg Lys Leu Phe Tyr
 245 250 255
 Val Ile Glu Thr Arg Gln Pro Arg Ala Arg Leu Leu Leu Thr Ala Ala
 260 265 270
 His Leu Leu Phe Val Ala Pro Gln His Asn Gln Ser Glu Ala Thr Gly
 275 280 285
 Ser Thr Ser Gly Gln Ala Leu Phe Ala Ser Asn Val Lys Pro Gly Gln
 290 295 300
 Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser
 305 310 315 320
 Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro
 325 330 335
 Leu Thr Ala Gln Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys
 340 345 350
 Tyr Ala Val Ile Glu Glu His Ser Trp Ala His Trp Ala Phe Ala Pro
 355 360 365
 Phe Arg Leu Ala Gln Gly Leu Leu Ala Ala Leu Cys Pro Asp Gly Ala
 370 375 380
 Ile Pro Thr Ala Ala Thr Thr Thr Thr Gly Ile His Trp Tyr Ser Arg
 385 390 395 400
 Leu Leu Tyr Arg Ile Gly Ser Trp Val Leu Asp Gly Asp Ala Leu His
 405 410 415
 Pro Leu Gly Met Val Ala Pro Ala Ser
 420 425

<210> 11
 <211> 396
 <212> PRT
 <213> Murine sp.

<400> 11
 Met Ala Leu Pro Ala Ser Leu Leu Pro Leu Cys Cys Leu Ala Leu Leu
 1 5 10 15
 Ala Leu Ser Ala Gln Ser Cys Gly Pro Gly Arg Gly Pro Val Gly Arg
 20 25 30
 Arg Arg Tyr Val Arg Lys Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe
 35 40 45

Val	Pro	Ser	Met	Pro	Glu	Arg	Thr	Leu	Gly	Ala	Ser	Gly	Pro	Ala	Glu	
	50					55					60					
Gly	Arg	Val	Thr	Arg	Gly	Ser	Glu	Arg	Phe	Arg	Asp	Leu	Val	Pro	Asn	
65					70					75					80	
Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Ser	Gly	Ala	Asp	
				85					90					95		
Arg	Leu	Met	Thr	Glu	Arg	Cys	Lys	Glu	Arg	Val	Asn	Ala	Leu	Ala	Ile	
			100					105					110			
Ala	Val	Met	Asn	Met	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly	
		115					120					125				
Trp	Asp	Glu	Asp	Gly	His	His	Ala	Gln	Asp	Ser	Leu	His	Tyr	Glu	Gly	
	130					135					140					
Arg	Ala	Leu	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Asn	Lys	Tyr	Gly	
145					150					155					160	
Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	
				165					170					175		
Glu	Ser	Arg	Asn	His	Ile	His	Val	Ser	Val	Lys	Ala	Asp	Asn	Ser	Leu	
			180					185					190			
Ala	Val	Arg	Ala	Gly	Gly	Cys	Phe	Pro	Gly	Asn	Ala	Thr	Val	Arg	Leu	
		195					200					205				
Arg	Ser	Gly	Glu	Arg	Lys	Gly	Leu	Arg	Glu	Leu	His	Arg	Gly	Asp	Trp	
	210					215					220					
Val	Leu	Ala	Ala	Asp	Ala	Ala	Gly	Arg	Val	Val	Pro	Thr	Pro	Val	Leu	
225					230					235					240	
Leu	Phe	Leu	Asp	Arg	Asp	Leu	Gln	Arg	Arg	Ala	Ser	Phe	Val	Ala	Val	
				245					250					255		
Glu	Thr	Glu	Arg	Pro	Pro	Arg	Lys	Leu	Leu	Leu	Thr	Pro	Trp	His	Leu	
			260					265					270			
Val	Phe	Ala	Ala	Arg	Gly	Pro	Ala	Pro	Ala	Pro	Gly	Asp	Phe	Ala	Pro	
	275						280					285				
Val	Phe	Ala	Arg	Arg	Leu	Arg	Ala	Gly	Asp	Ser	Val	Leu	Ala	Pro	Gly	
	290					295					300					
Gly	Asp	Ala	Leu	Gln	Pro	Ala	Arg	Val	Ala	Arg	Val	Ala	Arg	Glu	Glu	
305					310					315				320		
Ala	Val	Gly	Val	Phe	Ala	Pro	Leu	Thr	Ala	His	Gly	Thr	Leu	Leu	Val	
				325					330					335		
Asn	Asp	Val	Leu	Ala	Ser	Cys	Tyr	Ala	Val	Leu	Glu	Ser	His	Gln	Trp	
			340					345					350			

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
 355 360 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
 370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Met Gly
 385 390 395

<210> 12

<211> 411

<212> PRT

<213> Murine sp.

<400> 12

Met Ser Pro Ala Trp Leu Arg Pro Arg Leu Arg Phe Cys Leu Phe Leu
 1 5 10 15

Leu Leu Leu Leu Leu Val Pro Ala Ala Arg Gly Cys Gly Pro Gly Arg
 20 25 30

Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
 35 40 45

Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
 50 55 60

Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65 70 75 80

Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
 85 90 95

Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
 100 105 110

Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
 115 120 125

Val Thr Glu Gly Arg Asp Glu Asp Gly His His Ser Glu Glu Ser Leu
 130 135 140

His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg
 145 150 155 160

Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp
 165 170 175

Trp Val Tyr Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser
 180 185 190

Glu His Ser Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala
 195 200 205

Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala Leu Ser Ala Val Lys
 210 215 220

Pro Gly Asp Arg Val Leu Ala Met Gly Glu Asp Gly Thr Pro Thr Phe
 225 230 235 240
 Ser Asp Val Leu Ile Phe Leu Asp Arg Glu Pro Asn Arg Leu Arg Ala
 245 250 255
 Phe Gln Val Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr
 260 265 270
 Pro Ala His Leu Leu Phe Ile Ala Asp Asn His Thr Glu Pro Ala Ala
 275 280 285
 His Phe Arg Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val
 290 295 300
 Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val
 305 310 315 320
 Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro Leu Thr Arg His Gly
 325 330 335
 Thr Leu Val Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala
 340 345 350
 Asp His His Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe Pro
 355 360 365
 Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu Gly Val His Ser Tyr
 370 375 380
 Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Ser Thr
 385 390 395 400
 Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser
 405 410

<210> 13
 <211> 437
 <212> PRT
 <213> Murine sp.

<400> 13
 Met Leu Leu Leu Leu Ala Arg Cys Phe Leu Val Ile Leu Ala Ser Ser
 1 5 10 15
 Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly
 20 25 30
 Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe
 35 40 45
 Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu
 50 55 60
 Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn
 65 70 75 80

Tyr	Asn	Pro	Asp	Ile 85	Ile	Phe	Lys	Asp	Glu 90	Glu	Asn	Thr	Gly	Ala 95	Asp
Arg	Leu	Met	Thr 100	Gln	Arg	Cys	Lys	Asp 105	Lys	Leu	Asn	Ala	Leu 110	Ala	Ile
Ser	Val	Met 115	Asn	Gln	Trp	Pro	Gly 120	Val	Arg	Leu	Arg	Val 125	Thr	Glu	Gly
Trp	Asp 130	Glu	Asp	Gly	His 135	His	Ser	Glu	Glu	Ser	Leu 140	His	Tyr	Glu	Gly
Arg 145	Ala	Val	Asp	Ile	Thr 150	Thr	Ser	Asp	Arg	Asp 155	Arg	Ser	Lys	Tyr	Gly 160
Met	Leu	Ala	Arg	Leu 165	Ala	Val	Glu	Ala	Gly 170	Phe	Asp	Trp	Val	Tyr 175	Tyr
Glu	Ser	Lys	Ala 180	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn 190	Ser	Val
Ala	Ala	Lys 195	Ser	Gly	Gly	Cys	Phe 200	Pro	Gly	Ser	Ala	Thr 205	Val	His	Leu
Glu	Gln 210	Gly	Gly	Thr	Lys	Leu 215	Val	Lys	Asp	Leu	Arg 220	Pro	Gly	Asp	Arg
Val 225	Leu	Ala	Ala	Asp	Asp 230	Gln	Gly	Arg	Leu	Leu 235	Tyr	Ser	Asp	Phe	Leu 240
Thr	Phe	Leu	Asp 245	Arg	Asp	Glu	Gly	Ala	Lys 250	Lys	Val	Phe	Tyr	Val 255	Ile
Glu	Thr	Leu	Glu 260	Pro	Arg	Glu	Arg	Leu	Leu 265	Leu	Thr	Ala	Ala 270	His	Leu
Leu	Phe	Val 275	Ala	Pro	His	Asn	Asp 280	Ser	Gly	Pro	Thr	Pro 285	Gly	Pro	Ser
Ala 290	Leu	Phe	Ala	Ser	Arg	Val 295	Arg	Pro	Gly	Gln	Arg 300	Val	Tyr	Val	Val
Ala 305	Glu	Arg	Gly	Gly	Asp 310	Arg	Arg	Leu	Leu	Pro 315	Ala	Ala	Val	His	Ser 320
Val	Thr	Leu	Arg	Glu 325	Glu	Glu	Ala	Gly	Ala 330	Tyr	Ala	Pro	Leu	Thr 335	Ala
His	Gly	Thr	Ile 340	Leu	Ile	Asn	Arg	Val 345	Leu	Ala	Ser	Cys	Tyr 350	Ala	Val
Ile	Glu	Glu 355	His	Ser	Trp	Ala	His 360	Arg	Ala	Phe	Ala	Pro 365	Phe	Arg	Leu
Ala	His 370	Ala	Leu	Leu	Ala	Ala 375	Leu	Ala	Pro	Ala	Arg 380	Thr	Asp	Gly	Gly

Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly
385 390 395 400

Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His
405 410 415

Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met
420 425 430

Ala Val Lys Ser Ser
435

<210> 14

<211> 418

<212> PRT

<213> Brachydanio rerio

<400> 14

Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser
1 5 10 15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile
35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly
50 55 60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr
65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg
85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser
100 105 110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp
115 120 125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg
130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr
145 150 155 160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu
165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala
180 185 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln
195 200 205

Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val
 210 215 220
 Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met
 225 230 235 240
 Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu
 245 250 255
 Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu
 260 265 270
 Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala
 275 280 285
 Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp
 290 295 300
 Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu
 305 310 315 320
 Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val
 325 330 335
 Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu
 340 345 350
 Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser
 355 360 365
 Phe Leu Ser Pro Lys Thr Pro Ala Val Gly Pro Met Arg Leu Tyr Asn
 370 375 380
 Arg Arg Gly Ser Thr Gly Thr Pro Gly Ser Cys His Gln Met Gly Thr
 385 390 395 400
 Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn
 405 410 415

Ser Ser

<210> 15

<211> 475

<212> PRT

<213> Homo sapien

<220>

<221> MOD_RES

<222> (463)

<223> any or unknown amino acid

<400> 15

Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu
 1 5 10 15

Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys
 20 25 30

Arg	Arg	His	Pro	Lys	Lys	Leu	Thr	Pro	Leu	Ala	Tyr	Lys	Gln	Phe	Ile		
		35					40					45					
Pro	Asn	Val	Ala	Glu	Lys	Thr	Leu	Gly	Ala	Ser	Gly	Arg	Tyr	Glu	Gly		
	50					55					60						
Lys	Ile	Ser	Arg	Asn	Ser	Glu	Arg	Phe	Lys	Glu	Leu	Thr	Pro	Asn	Tyr		
65					70					75					80		
Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg		
				85					90					95			
Leu	Met	Thr	Gln	Arg	Cys	Lys	Asp	Lys	Leu	Asn	Ala	Leu	Ala	Ile	Ser		
			100					105					110				
Val	Met	Asn	Gln	Trp	Pro	Gly	Val	Lys	Leu	Arg	Val	Thr	Glu	Gly	Trp		
	115					120						125					
Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg		
130						135					140						
Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Ser	Lys	Tyr	Gly	Met		
145					150					155					160		
Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu		
			165					170						175			
Ser	Lys	Ala	His	Ile	His	Cys	Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala		
			180					185					190				
Ala	Lys	Ser	Gly	Gly	Cys	Phe	Pro	Gly	Ser	Ala	Thr	Val	His	Leu	Glu		
	195						200					205					
Gln	Gly	Gly	Thr	Lys	Leu	Val	Lys	Asp	Leu	Ser	Pro	Gly	Asp	Arg	Val		
210						215					220						
Leu	Ala	Ala	Asp	Asp	Gln	Gly	Arg	Leu	Leu	Tyr	Ser	Asp	Phe	Leu	Thr		
225					230					235					240		
Phe	Leu	Asp	Arg	Asp	Asp	Gly	Ala	Lys	Lys	Val	Phe	Tyr	Val	Ile	Glu		
				245					250					255			
Thr	Arg	Glu	Pro	Arg	Glu	Arg	Leu	Leu	Leu	Thr	Ala	Ala	His	Leu	Leu		
			260					265						270			
Phe	Val	Ala	Pro	His	Asn	Asp	Ser	Ala	Thr	Gly	Glu	Pro	Glu	Ala	Ser		
	275						280					285					
Ser	Gly	Ser	Gly	Pro	Pro	Ser	Gly	Gly	Ala	Leu	Gly	Pro	Arg	Ala	Leu		
290						295					300						
Phe	Ala	Ser	Arg	Val	Arg	Pro	Gly	Gln	Arg	Val	Tyr	Val	Val	Ala	Glu		
305					310					315					320		
Arg	Asp	Gly	Asp	Arg	Arg	Leu	Leu	Pro	Ala	Ala	Val	His	Ser	Val	Thr		
				325					330					335			

Leu Ser Glu Glu Ala Ala Gly Ala Tyr Ala Pro Leu Thr Ala Gln Gly
 340 345 350
 Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu
 355 360 365
 Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His
 370 375 380
 Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp
 385 390 395 400
 Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr
 405 410 415
 Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile
 420 425 430
 His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp
 435 440 445
 Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser Xaa Ser
 450 455 460
 Arg Gly Ala Gly Gly Gly Ala Arg Glu Gly Ala
 465 470 475

<210> 16
 <211> 411
 <212> PRT
 <213> Homo sapien

<400> 16
 Met Ser Pro Ala Arg Leu Arg Pro Arg Leu His Phe Cys Leu Val Leu
 1 5 10 15
 Leu Leu Leu Leu Val Val Pro Ala Ala Trp Gly Cys Gly Pro Gly Arg
 20 25 30
 Val Val Gly Ser Arg Arg Arg Pro Pro Arg Lys Leu Val Pro Leu Ala
 35 40 45
 Tyr Lys Gln Phe Ser Pro Asn Val Pro Glu Lys Thr Leu Gly Ala Ser
 50 55 60
 Gly Arg Tyr Glu Gly Lys Ile Ala Arg Ser Ser Glu Arg Phe Lys Glu
 65 70 75 80
 Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn
 85 90 95
 Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn
 100 105 110
 Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg
 115 120 125

Val	Thr	Glu	Gly	Trp	Asp	Glu	Asp	Gly	His	His	Ser	Glu	Glu	Ser	Leu	130	135	140
His	Tyr	Glu	Gly	Arg	Ala	Val	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	145	150	155
Asn	Lys	Tyr	Gly	Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	165	170	175
Trp	Val	Tyr	Tyr	Glu	Ser	Lys	Ala	His	Val	His	Cys	Ser	Val	Lys	Ser	180	185	190
Glu	His	Ser	Ala	Ala	Ala	Lys	Thr	Gly	Gly	Cys	Phe	Pro	Ala	Gly	Ala	195	200	205
Gln	Val	Arg	Leu	Glu	Ser	Gly	Ala	Arg	Val	Ala	Leu	Ser	Ala	Val	Arg	210	215	220
Pro	Gly	Asp	Arg	Val	Leu	Ala	Met	Gly	Glu	Asp	Gly	Ser	Pro	Thr	Phe	225	230	235
Ser	Asp	Val	Leu	Ile	Phe	Leu	Asp	Arg	Glu	Pro	His	Arg	Leu	Arg	Ala	245	250	255
Phe	Gln	Val	Ile	Glu	Thr	Gln	Asp	Pro	Pro	Arg	Arg	Leu	Ala	Leu	Thr	260	265	270
Pro	Ala	His	Leu	Leu	Phe	Thr	Ala	Asp	Asn	His	Thr	Glu	Pro	Ala	Ala	275	280	285
Arg	Phe	Arg	Ala	Thr	Phe	Ala	Ser	His	Val	Gln	Pro	Gly	Gln	Tyr	Val	290	295	300
Leu	Val	Ala	Gly	Val	Pro	Gly	Leu	Gln	Pro	Ala	Arg	Val	Ala	Ala	Val	305	310	315
Ser	Thr	His	Val	Ala	Leu	Gly	Ala	Tyr	Ala	Pro	Leu	Thr	Lys	His	Gly	325	330	335
Thr	Leu	Val	Val	Glu	Asp	Val	Val	Ala	Ser	Cys	Phe	Ala	Ala	Val	Ala	340	345	350
Asp	His	His	Leu	Ala	Gln	Leu	Ala	Phe	Trp	Pro	Leu	Arg	Leu	Phe	His	355	360	365
Ser	Leu	Ala	Trp	Gly	Ser	Trp	Thr	Pro	Gly	Glu	Gly	Val	His	Trp	Tyr	370	375	380
Pro	Gln	Leu	Leu	Tyr	Arg	Leu	Gly	Arg	Leu	Leu	Leu	Glu	Glu	Gly	Ser	385	390	395
Phe	His	Pro	Leu	Gly	Met	Ser	Gly	Ala	Gly	Ser						405	410	

<210> 17
 <211> 396
 <212> PRT
 <213> Homo sapien

<400> 17

Met	Ala	Leu	Leu	Thr	Asn	Leu	Leu	Pro	Leu	Cys	Cys	Leu	Ala	Leu	Leu
1				5					10					15	
Ala	Leu	Pro	Ala	Gln	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Pro	Val	Gly	Arg
			20					25					30		
Arg	Arg	Tyr	Ala	Arg	Lys	Gln	Leu	Val	Pro	Leu	Leu	Tyr	Lys	Gln	Phe
		35					40					45			
Val	Pro	Gly	Val	Pro	Glu	Arg	Thr	Leu	Gly	Ala	Ser	Gly	Pro	Ala	Glu
	50					55					60				
Gly	Arg	Val	Ala	Arg	Gly	Ser	Glu	Arg	Phe	Arg	Asp	Leu	Val	Pro	Asn
65					70					75					80
Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys	Asp	Glu	Glu	Asn	Ser	Gly	Ala	Asp
				85					90					95	
Arg	Leu	Met	Thr	Glu	Arg	Cys	Lys	Glu	Arg	Val	Asn	Ala	Leu	Ala	Ile
			100					105					110		
Ala	Val	Met	Asn	Met	Trp	Pro	Gly	Val	Arg	Leu	Arg	Val	Thr	Glu	Gly
		115					120					125			
Trp	Asp	Glu	Asp	Gly	His	His	Ala	Gln	Asp	Ser	Leu	His	Tyr	Glu	Gly
	130					135					140				
Arg	Ala	Leu	Asp	Ile	Thr	Thr	Ser	Asp	Arg	Asp	Arg	Asn	Lys	Tyr	Gly
145					150				155						160
Leu	Leu	Ala	Arg	Leu	Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr
				165					170					175	
Glu	Ser	Arg	Asn	His	Val	His	Val	Ser	Val	Lys	Ala	Asp	Asn	Ser	Leu
			180					185					190		
Ala	Val	Arg	Ala	Gly	Gly	Cys	Phe	Pro	Gly	Asn	Ala	Thr	Val	Arg	Leu
		195					200					205			
Trp	Ser	Gly	Glu	Arg	Lys	Gly	Leu	Arg	Glu	Leu	His	Arg	Gly	Asp	Trp
	210					215					220				
Val	Leu	Ala	Ala	Asp	Ala	Ser	Gly	Arg	Val	Val	Pro	Thr	Pro	Val	Leu
225					230					235					240
Leu	Phe	Leu	Asp	Arg	Asp	Leu	Gln	Arg	Arg	Ala	Ser	Phe	Val	Ala	Val
				245					250					255	
Glu	Thr	Glu	Trp	Pro	Pro	Arg	Lys	Leu	Leu	Leu	Thr	Pro	Trp	His	Leu
			260					265					270		
Val	Phe	Ala	Ala	Arg	Gly	Pro	Ala	Pro	Ala	Pro	Gly	Asp	Phe	Ala	Pro
		275					280					285			
Val	Phe	Ala	Arg	Arg	Leu	Arg	Ala	Gly	Asp	Ser	Val	Leu	Ala	Pro	Gly
						295					300				

Gly Asp Ala Leu Arg Pro Ala Arg Val Ala Arg Val Ala Arg Glu Glu
305 310 315 320

Ala Val Gly Val Phe Ala Pro Leu Thr Ala His Gly Thr Leu Leu Val
325 330 335

Asn Asp Val Leu Ala Ser Cys Tyr Ala Val Leu Glu Ser His Gln Trp
340 345 350

Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala
355 360 365

Leu Leu Pro Gly Gly Ala Val Gln Pro Thr Gly Met His Trp Tyr Ser
370 375 380

Arg Leu Leu Tyr Arg Leu Ala Glu Glu Leu Leu Gly
385 390 395

<210> 18

<211> 416

<212> PRT

<213> Brachydanio rerio

<400> 18

Met Asp Val Arg Leu His Leu Lys Gln Phe Ala Leu Leu Cys Phe Ile
1 5 10 15

Ser Leu Leu Leu Thr Pro Cys Gly Leu Ala Cys Gly Pro Gly Arg Gly
20 25 30

Tyr Gly Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys
35 40 45

Gln Phe Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Lys
50 55 60

Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Ile
65 70 75 80

Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Asn
85 90 95

Ala Asp Arg Leu Met Thr Lys Arg Cys Lys Asp Lys Leu Asn Ser Leu
100 105 110

Ala Ile Ser Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr
115 120 125

Glu Gly Trp Asp Glu Asp Gly His His Leu Glu Glu Ser Leu His Tyr
130 135 140

Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys
145 150 155 160

Tyr Gly Met Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val
165 170 175

Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn
 180 185 190
 Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Gly Thr Val
 195 200 205
 Thr Leu Gly Asp Gly Thr Arg Lys Pro Ile Lys Asp Leu Lys Val Gly
 210 215 220
 Asp Arg Val Leu Ala Ala Asp Glu Lys Gly Asn Val Leu Ile Ser Asp
 225 230 235 240
 Phe Ile Met Phe Ile Asp His Asp Pro Thr Thr Arg Arg Gln Phe Ile
 245 250 255
 Val Ile Glu Thr Ser Glu Pro Phe Thr Lys Leu Thr Leu Thr Ala Ala
 260 265 270
 His Leu Val Phe Val Gly Asn Ser Ser Ala Ala Ser Gly Ile Thr Ala
 275 280 285
 Thr Phe Ala Ser Asn Val Lys Pro Gly Asp Thr Val Leu Val Trp Glu
 290 295 300
 Asp Thr Cys Glu Ser Leu Lys Ser Val Thr Val Lys Arg Ile Tyr Thr
 305 310 315 320
 Glu Glu His Glu Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile
 325 330 335
 Ile Val Asp Gln Val Leu Ala Ser Cys Tyr Ala Val Ile Glu Asn His
 340 345 350
 Lys Trp Ala His Trp Ala Phe Ala Pro Val Arg Leu Cys His Lys Leu
 355 360 365
 Met Thr Trp Leu Phe Pro Ala Arg Glu Ser Asn Val Asn Phe Gln Glu
 370 375 380
 Asp Gly Ile His Trp Tyr Ser Asn Met Leu Phe His Ile Gly Ser Trp
 385 390 395 400
 Leu Leu Asp Arg Asp Ser Phe His Pro Leu Gly Ile Leu His Leu Ser
 405 410 415

<210> 19

<211> 1416

<212> DNA

<213> Drosophila sp.

<220>

<221> CDS

<222> (1)..(1413)

<400> 19

atg gat aac cac agc tca gtg cct tgg gcc agt gcc gcc agt gtc acc
 Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
 1 5 10 15

tgt	ctc	tcc	ctg	gga	tgc	caa	atg	cca	cag	ttc	cag	ttc	cag	ttc	cag	96
Cys	Leu	Ser	Leu	Gly	Cys	Gln	Met	Pro	Gln	Phe	Gln	Phe	Gln	Phe	Gln	
			20					25					30			
ctc	caa	atc	cgc	agc	gag	ctc	cat	ctc	cgc	aag	ccc	gca	aga	aga	acg	144
Leu	Gln	Ile	Arg	Ser	Glu	Leu	His	Leu	Arg	Lys	Pro	Ala	Arg	Arg	Thr	
		35					40					45				
caa	acg	atg	cgc	cac	att	gcg	cat	acg	cag	cgt	tgc	ctc	agc	agg	ctg	192
Gln	Thr	Met	Arg	His	Ile	Ala	His	Thr	Gln	Arg	Cys	Leu	Ser	Arg	Leu	
	50					55					60					
acc	tct	ctg	gtg	gcc	ctg	ctg	ctg	atc	gtc	ttg	ccg	atg	gtc	ttt	agc	240
Thr	Ser	Leu	Val	Ala	Leu	Leu	Leu	Ile	Val	Leu	Pro	Met	Val	Phe	Ser	
65					70				75						80	
ccg	gct	cac	agc	tgc	ggg	cct	ggc	cga	gga	ttg	ggg	cgt	cat	agg	gcg	288
Pro	Ala	His	Ser	Cys	Gly	Pro	Gly	Arg	Gly	Leu	Gly	Arg	His	Arg	Ala	
				85					90					95		
cgc	aac	ctg	tat	ccg	ctg	gtc	ctc	aag	cag	aca	att	ccc	aat	cta	tcc	336
Arg	Asn	Leu	Tyr	Pro	Leu	Val	Leu	Lys	Gln	Thr	Ile	Pro	Asn	Leu	Ser	
			100					105					110			
gag	tac	acg	aac	agc	gcc	tcc	gga	cct	ctg	gag	ggg	gtg	atc	cgt	cgg	384
Glu	Tyr	Thr	Asn	Ser	Ala	Ser	Gly	Pro	Leu	Glu	Gly	Val	Ile	Arg	Arg	
		115					120					125				
gat	tcg	ccc	aaa	ttc	aag	gac	ctc	gtg	ccc	aac	tac	aac	agg	gac	atc	432
Asp	Ser	Pro	Lys	Phe	Lys	Asp	Leu	Val	Pro	Asn	Tyr	Asn	Arg	Asp	Ile	
	130					135					140					
ctt	ttc	cgt	gac	gag	gaa	ggc	acc	gga	gcg	gat	ggc	ttg	atg	agc	aag	480
Leu	Phe	Arg	Asp	Glu	Glu	Gly	Thr	Gly	Ala	Asp	Gly	Leu	Met	Ser	Lys	
145					150				155						160	
cgc	tgc	aag	gag	aag	cta	aac	gtg	ctg	gcc	tac	tcg	gtg	atg	aac	gaa	528
Arg	Cys	Lys	Glu	Lys	Leu	Asn	Val	Leu	Ala	Tyr	Ser	Val	Met	Asn	Glu	
				165				170						175		
tgg	ccc	ggc	atc	cgg	ctg	ctg	gtc	acc	gag	agc	tgg	gac	gag	gac	tac	576
Trp	Pro	Gly	Ile	Arg	Leu	Leu	Val	Thr	Glu	Ser	Trp	Asp	Glu	Asp	Tyr	
			180				185						190			
cat	cac	ggc	cag	gag	tcg	ctc	cac	tac	gag	ggc	cga	gcg	gtg	acc	att	624
His	His	Gly	Gln	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	Ala	Val	Thr	Ile	
		195					200					205				
gcc	acc	tcc	gat	cgc	gac	cag	tcc	aaa	tac	ggc	atg	ctc	gct	cgc	ctg	672
Ala	Thr	Ser	Asp	Arg	Asp	Gln	Ser	Lys	Tyr	Gly	Met	Leu	Ala	Arg	Leu	
	210					215					220					
gcc	gtc	gag	gct	gga	ttc	gat	tgg	gtc	tcc	tac	gtc	agc	agg	cgc	cac	720
Ala	Val	Glu	Ala	Gly	Phe	Asp	Trp	Val	Ser	Tyr	Val	Ser	Arg	Arg	His	
225					230					235					240	

atc tac tgc tcc gtc aag tca gat tgc tgc atc agt tcc cac gtg cac	768
Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His	
245 250 255	
ggc tgc ttc acg ccg gag agc aca gcg ctg ctg gag agt gga gtc cgg	816
Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg	
260 265 270	
aag ccg ctc ggc gag ctc tct atc gga gat cgt gtt ttg agc atg acc	864
Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr	
275 280 285	
gcc aac gga cag gcc gtc tac agc gaa gtg atc ctc ttc atg gac cgc	912
Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg	
290 295 300	
aac ctc gag cag atg caa aac ttt gtg cag ctg cac acg gac ggt gga	960
Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly	
305 310 315 320	
gca gtg ctc acg gtg acg ccg gct cac ctg gtt agc gtt tgg cag ccg	1008
Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro	
325 330 335	
gag agc cag aag ctc acg ttt gtg ttt gcg cat cgc atc gag gag aag	1056
Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys	
340 345 350	
aac cag gtg ctc gta cgg gat gtg gag acg ggc gag ctg agg ccc cag	1104
Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln	
355 360 365	
cga gtg gtc aag ttg ggc agt gtg cgc agt aag ggc gtg gtc gcg ccg	1152
Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro	
370 375 380	
ctg acc cgc gag ggc acc att gtg gtc aac tgc gtg gcc gcc agt tgc	1200
Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys	
385 390 395 400	
tat gcg gtg atc aac agt cag tgc ctg gcc cac tgg gga ctg gct ccc	1248
Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro	
405 410 415	
atg cgc ctg ctg tcc acg ctg gag gcg tgg ctg ccc gcc aag gag cag	1296
Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln	
420 425 430	
ttg cac agt tgc ccg aag gtg gtg agc tgc gcg cag cag cag aat ggc	1344
Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly	
435 440 445	
atc cat tgg tat gcc aat gcg ctc tac aag gtc aag gac tac gtg ctg	1392
Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu	
450 455 460	

ccg cag agc tgg cgc cac gat tga
 Pro Gln Ser Trp Arg His Asp
 465 470

1416

<210> 20
 <211> 471
 <212> PRT
 <213> Drosophila sp.

<400> 20
 Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr
 1 5 10 15
 Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln
 20 25 30
 Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr
 35 40 45
 Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu
 50 55 60
 Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser
 65 70 75 80
 Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala
 85 90 95
 Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser
 100 105 110
 Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg
 115 120 125
 Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile
 130 135 140
 Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys
 145 150 155 160
 Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu
 165 170 175
 Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr
 180 185 190
 His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile
 195 200 205
 Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu
 210 215 220
 Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His
 225 230 235 240
 Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His
 245 250 255

Gly	Cys	Phe	Thr 260	Pro	Glu	Ser	Thr	Ala 265	Leu	Leu	Glu	Ser	Gly 270	Val	Arg
Lys	Pro	Leu 275	Gly	Glu	Leu	Ser	Ile 280	Gly	Asp	Arg	Val	Leu 285	Ser	Met	Thr
Ala	Asn 290	Gly	Gln	Ala	Val	Tyr 295	Ser	Glu	Val	Ile	Leu 300	Phe	Met	Asp	Arg
Asn 305	Leu	Glu	Gln	Met	Gln 310	Asn	Phe	Val	Gln	Leu 315	His	Thr	Asp	Gly	Gly 320
Ala	Val	Leu	Thr	Val 325	Thr	Pro	Ala	His	Leu 330	Val	Ser	Val	Trp	Gln 335	Pro
Glu	Ser	Gln	Lys 340	Leu	Thr	Phe	Val	Phe 345	Ala	His	Arg	Ile	Glu 350	Glu	Lys
Asn	Gln	Val 355	Leu	Val	Arg	Asp	Val 360	Glu	Thr	Gly	Glu	Leu 365	Arg	Pro	Gln
Arg	Val 370	Val	Lys	Leu	Gly	Ser 375	Val	Arg	Ser	Lys	Gly 380	Val	Val	Ala	Pro
Leu 385	Thr	Arg	Glu	Gly	Thr 390	Ile	Val	Val	Asn	Ser 395	Val	Ala	Ala	Ser	Cys 400
Tyr	Ala	Val	Ile	Asn 405	Ser	Gln	Ser	Leu	Ala 410	His	Trp	Gly	Leu	Ala 415	Pro
Met	Arg	Leu	Leu 420	Ser	Thr	Leu	Glu	Ala 425	Trp	Leu	Pro	Ala	Lys 430	Glu	Gln
Leu	His	Ser 435	Ser	Pro	Lys	Val	Val 440	Ser	Ser	Ala	Gln	Gln 445	Gln	Asn	Gly
Ile	His 450	Trp	Tyr	Ala	Asn	Ala 455	Leu	Tyr	Lys	Val	Lys 460	Asp	Tyr	Val	Leu
Pro 465	Gln	Ser	Trp	Arg	His 470	Asp									

<210> 21

<211> 221

<212> PRT

<213> Artificial Sequence

$\langle 220 \rangle$

<223> Description of Artificial Sequence: degenerate polypeptide sequence

<220>

<221> MOD RES

<222> 7

<223> Gly, Ala, Val, Leu, Ile, Phe, Tyr or Trp

<220>
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<222> 9
<223> Arg, His or Lys

<220>
<221> MOD_RES
<222> 44
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> MOD_RES
<222> 85
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> MOD_RES
<222> 93
<223> Lys, Arg, His, Asn or Gln

<220>
<221> MOD_RES
<222> 98
<223> Lys, Arg or His

<220>
<221> MOD_RES
<222> 112
<223> Ser, Thr, Tyr, Trp or Phe

<220>
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<222> 132
<223> Lys, Arg or His

<220>
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<222> 137
<223> Met, Cys, Ser or Thr

<220>
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<222> 139
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> MOD_RES
<222> 181
<223> Leu, Val, Met, Thr or Ser

<220>
<221> MOD_RES
<222> 183
<223> His, Phe, Tyr, Ser, Thr, Met or Cys

<220>
<221> MOD_RES
<222> 185

<223> Gln, Asn, Glu, or Asp

<220>
<221> MOD_RES
<222> 186
<223> His, Phe, Tyr, Thr, Gln, Asn, Glu or Asp

<220>
<221> MOD_RES
<222> 189
<223> Gln, Asn, Glu, Asp, Thr, Ser, Met or Cys

<220>
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<222> 191
<223> Ala, Gly, Cys, Leu, Val or Met

<220>
<221> MOD_RES
<222> 196
<223> Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser, Thr or Cys

<220>
<221> MOD_RES
<222> 200
<223> Arg, Lys, Met or Ile

<220>
<221> MOD_RES
<222> 206
<223> Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr or Met

<220>
<221> MOD_RES
<222> 207
<223> Ala, Gly, Cys, Asp, Asn, Glu or Gln

<220>
<221> MOD_RES
<222> 209
<223> Arg, Lys, Met, Ile, Asn, Asp, Glu or Gln

<220>
<221> MOD_RES
<222> 211
<223> Leu, Val, Met or Ile

<220>
<221> MOD_RES
<222> 212
<223> Phe, Tyr, Thr, His or Trp

<220>
<221> MOD_RES
<222> 216
<223> Ile, Val, Leu or Met

<220>

<221> MOD_RES

<222> 217

<223> Met, Cys, Ile, Leu, Val, Thr or Ser

<220>

<221> MOD_RES

<222> 219

<223> Leu, Val, Met, Thr or Ser

<220>

<223> each Xaa may also be any amino acid.

<400> 21

Cys	Gly	Pro	Gly	Arg	Gly	Xaa	Gly	Xaa	Arg	Arg	His	Pro	Lys	Lys	Leu
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Thr	Pro	Leu	Ala	Tyr	Lys	Gln	Phe	Ile	Pro	Asn	Val	Ala	Glu	Lys	Thr
			20					25					30		

Leu	Gly	Ala	Ser	Gly	Arg	Tyr	Glu	Gly	Lys	Ile	Xaa	Arg	Asn	Ser	Glu
		35					40					45			

Arg	Phe	Lys	Glu	Leu	Thr	Pro	Asn	Tyr	Asn	Pro	Asp	Ile	Ile	Phe	Lys
	50					55					60				

Asp	Glu	Glu	Asn	Thr	Gly	Ala	Asp	Arg	Leu	Met	Thr	Gln	Arg	Cys	Lys
65					70					75					80

Asp	Lys	Leu	Asn	Xaa	Leu	Ala	Ile	Ser	Val	Met	Asn	Xaa	Trp	Pro	Gly
			85						90					95	

Val	Xaa	Leu	Arg	Val	Thr	Glu	Gly	Trp	Asp	Glu	Asp	Gly	His	His	Xaa
		100						105					110		

Glu	Glu	Ser	Leu	His	Tyr	Glu	Gly	Arg	Ala	Val	Asp	Ile	Thr	Thr	Ser
		115					120					125			

Asp	Arg	Asp	Xaa	Ser	Lys	Tyr	Gly	Xaa	Leu	Xaa	Arg	Leu	Ala	Val	Glu
	130					135					140				

Ala	Gly	Phe	Asp	Trp	Val	Tyr	Tyr	Glu	Ser	Lys	Ala	His	Ile	His	Cys
145					150					155					160

Ser	Val	Lys	Ala	Glu	Asn	Ser	Val	Ala	Ala	Lys	Ser	Gly	Gly	Cys	Phe
			165						170					175	

Pro	Gly	Ser	Ala	Xaa	Val	Xaa	Leu	Xaa	Xaa	Gly	Gly	Xaa	Lys	Xaa	Val
			180					185					190		

Lys	Asp	Leu	Xaa	Pro	Gly	Asp	Xaa	Val	Leu	Ala	Ala	Asp	Xaa	Xaa	Gly
		195				200						205			

Xaa	Leu	Xaa	Xaa	Ser	Asp	Phe	Xaa	Xaa	Phe	Xaa	Asp	Arg
	210					215					220	

<210> 22

<211> 167

<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: degenerate
polypeptide sequence

<220>
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<222> 7
<223> Gly, Ala, Val, Leu, Ile, Pro, Phe or Tyr

<220>
<221> MOD_RES
<222> 8
<223> Gly, Ala, Val, Leu or Ile

<220>
<221> MOD_RES
<222> 9
<223> Gly, Ala, Val, Leu, Ile, Lys, His or Arg

<220>
<221> MOD_RES
<222> 12
<223> Lys, Arg or His

<220>
<221> MOD_RES
<222> 13
<223> Phe, Trp, Tyr or an amino acid gap

<220>
<221> MOD_RES
<222> 14
<223> Gly, Ala, Val, Leu, Ile or an amino acid gap

<220>
<221> MOD_RES
<222> 17
<223> Asn, Gln, His, Arg or Lys

<220>
<221> MOD_RES
<222> 19
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> MOD_RES
<222> 22
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> MOD_RES
<222> 27
<223> Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>

<221> MOD_RES
<222> 29
<223> Ser, Thr, Gln or Asn

<220>
<221> MOD_RES
<222> 30
<223> Met, Cys, Gly, Ala, Val, Leu, Ile, Ser or Thr

<220>
<221> MOD_RES
<222> 31
<223> Gly, Ala, Val, Leu, Ile or Pro

<220>
<221> MOD_RES
<222> 33
<223> Arg, His or Lys

<220>
<221> MOD_RES
<222> 40
<223> Gly, Ala, Val, Leu, Ile, Pro, Arg, His or Lys

<220>
<221> MOD_RES
<222> 41
<223> Gly, Ala, Val, Leu, Ile, Phe or Tyr

<220>
<221> MOD_RES
<222> 44
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<220>
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<222> 46
<223> Thr or Ser

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<223> Arg, His or Lys

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<221> MOD_RES
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<222> 95
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<222> 100
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<222> 114
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<222> 116
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<221> MOD_RES
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<223> Asp or Glu

<400> 22

Cys Gly Pro Gly Arg Gly Xaa Xaa Xaa Arg Arg Xaa Xaa Xaa Pro Lys
 1 5 10 15

Xaa Leu Xaa Pro Leu Xaa Tyr Lys Gln Phe Xaa Pro Xaa Xaa Xaa Glu
 20 25 30

Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa
 35 40 45

Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile
 50 55 60

Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg
 65 70 75 80

Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp
 85 90 95

Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His
 100 105 110

His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr
 115 120 125

Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala
 130 135 140

Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Xaa Xaa His Xaa
 145 150 155 160

His Xaa Ser Val Lys Xaa Xaa
 165

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<211> 74

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: primer

<400> 23

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aaatcgatgc gcgc

74

<210> 24

<211> 74

<212> DNA

<213> Artificial Sequence

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 cgggatccgc gcgc 74

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 <212> DNA
 <213> Artificial Sequence

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 activation construct

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 ggttcgaatc cttccccac caccatcact ttcaaaagtc cgaaagaatc tgctccctgc 120
 ttgtgtgttg gaggtcgctg agtagtgccg gagtaaaatt taagctacaa caaggcaagg 180
 cttgaccgac aattgcatga agaactctgct taggggttagg cgttttgcgc tgcttcgcga 240
 tgtacggggc agatatacgc gttgacattg attattgact agttattaat agtaatcaat 300
 tacgggggtca ttagttcata gcccatatat ggagttccgc gttacataac ttacggtaaa 360
 tggcccgccct ggctgaccgc ccaacgaccc ccgcccattg acgtcaataa tgacgtatgt 420
 tcccatagta acgccaatag ggactttcca ttgacgtcaa tgggtggact atttacggta 480
 aactgcccac ttggcagtac atcaagtgtg tcatatgccg agtacgcccc ctattgacgt 540
 caatgacggg aaatggcccg cctggcatta tgcccagtac atgaccttat gggactttcc 600
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 gtacatcaat gggcggtgat agcgggtttga ctcacgggga tttccaagtc tccaccccat 720
 tgacgtcaat gggagtttgt tttggcacca aaatcaacgg gactttccaa aatgtcgtaa 780
 caactccgcc ccattgacgc aaatgggcgg taggcgtgta cgggtgggagg tctatataag 840
 cagagctctc tggctaacta gagaaccac tgcttactgg cttatcgaaa ttaatacgac 900
 tcactatagg gagaccaag cttggtaccg agctcggatc gatctgggaa agcgcaagag 960
 agagcgaca cgcacacacc cgccgcgcgc actcgg 996

<210> 26
 <211> 26
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: antisense
 construct

<400> 26
 gtcctggcgc cgccgccgcc gtcgcc 26

<210> 27
 <211> 26
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: antisense
 construct

<400> 27
 ttccgatgac cggcctttcg cggatga 26

<210> 28
 <211> 26
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: antisense
 construct

<400> 28
 gtgcacggaa aggtgcaggc cacact 26

<210> 29
 <211> 15
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: primer

<400> 29
 ggctccggta tgtgc 15

<210> 30
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 <212> DNA
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<220>
 <223> Description of Artificial Sequence: primer

<400> 30
 ggggtacttc agggt 15

<210> 31
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<223> Description of Artificial Sequence: primer

<400> 31

cattggcagg aggagttgat tgtgg

25

<210> 32

<211> 25

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: primer

<400> 32

agcacctttt gaggaggatt tgggg

25